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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/148,234	09/04/98	MOUTSATSOS I	GI5298A

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EXAMINER	
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ART UNIT	PAPER NUMBER
1636	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

File 4/4

Office Action Summary

Application No.	Applicant(s)
09/148,234	Moutsatos et al.
Examiner	**Art Unit**
WILLIAM SANDALS	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 5, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *11, 12, 14-17, and 19-23* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *11, 12, 14-17, and 19-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☒ The proposed drawing correction filed on *Oct. 8, 1998* is: a) ☒ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on April 9, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/148,234 is acceptable and a CPA has been established. An action on the CPA follows.

Response to Arguments

2. Amendments to the claims in Paper No. 15, filed September 5, 2000 have overcome the rejection of claims 11-23 under 35 USC 112, first paragraph in the previous office action, and the rejection is withdrawn.

3. Arguments presented in Paper No. 15 regarding the rejection of claims 11-23 under 35 USC 103 have been fully considered but they are not persuasive. The response to the arguments is contained in the rejection repeated below.

Drawings

4. The drawings as submitted on October 8, 1998, have been approved by the draftsman.

Specification

5. The use of the trademarks NONIDET, TRITON, RNAZOL B, DE CAL, RNEASY MINI KIT and CHOLESTATR (" CHOLESTATR appears to be a typograhical error for the trademark term "COLLASTATR") have been found in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

the full scope of the claims.

Claim Objections

6. Claim 15 is objected to because of the following informalities: Claim 15 depends from cancelled claim 1. Claim 15 has been examined with the assumption that claim 15 depends from claim 11. Appropriate correction is required.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 11, 12, 14-17, and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,763,416 (of record) or WO 96/39431 (of record) in view of US Pat No. 5,645,084 (of record), US Pat No. 5,700,774 (of record) and US 6,048,964.

US Pat No. 5,763,416 taught (see especially columns 3-5 and 7-12) or WO 96/39431 taught (see especially pages 2, 15-16, 19, 33 and the claims) a method of producing cultured or bone marrow stromal cells for implantation at the site of a bone infirmity by transfecting the cells with recombinant bone morphogenic protein. US Pat No. 5,763,416 at column 3 suggests the use of PTH in the method, where BMP and PTH can be coexpressed in the target cells, and identifies the requirement of BMP and/or PTH receptors in the target cells. US Pat No. 5,763,416 at column 4 suggests the use of bone progenitor cells. WO 96/39431 taught that the bone morphogenic protein was BMP-10. US Pat No. 5,763,416 taught that the method may be practiced with BMP-2 as well as other bone morphogenetic proteins.

US Pat No. 5,763,416 did not teach that the cells coexpress PTH and a PTH receptor. WO 96/39431 did not teach that the BMP was BMP-2, nor that the cells were progenitor cells, nor that the cells coexpress PTH and a PTH receptor.

US Pat No. 5,645,084 taught (see especially column 4) that BMP-2 is closely related to the BMP-10 of WO 96/39431, where BMP-2 and BMP-10 may be used interchangeably in a method of use for treating a bone infirmity.

US Pat No. 5,700,774 taught (see especially columns 1 and 2) the interchangeability of BMP-2 and BMP-10, as well as the use of PTH and PTH receptor in cells in need of treatment with BMP-2, where the affected bone-generating target cells are known to express PTH receptor.

US 6,048,964 (see especially the abstract, summary and columns 5-8) taught that recombinant DNA sequences were used to produce the BMP-2 protein in cells, and that BMP-2 was known to produce differentiation and proliferation of bone progenitor cells.

It would have been obvious to one of ordinary skill in the art at the time of filing of the instant specification to combine the method of producing cultured or bone marrow progenitor cells for implantation at the site of a bone infirmity by transfecting the cells with recombinant bone morphogenic protein of US Pat No. 5,763,416, or the method of producing cultured cells for implantation at the site of a bone infirmity by transfecting the cells with recombinant bone morphogenic protein of WO 96/39431 with the interchangeable BMP-2 protein of US Pat No. 5,645,084 or the interchangeable BMP-2 protein of US Pat No. 5,700,774 where PTH and PTH receptor are known to be produced in the target cells of the method because all of the references taught the treatment of bone infirmities with BMP's, and the BMP's are shown to be interchangeable for the use of treating a bone infirmity, and PTH and PTH receptor are known to be expressed in the target cells.

One of ordinary skill in the art would have been motivated at the time of filing of the instant specification to combine the method of producing cultured or bone marrow progenitor cells for implantation at the site of a bone infirmity by transfecting the cells with recombinant

bone morphogenic protein of US Pat No. 5,763,416, where US Pat No. 5,763,416 recites at column 4, "this invention provides advantageous methods for using genes to stimulate bone progenitor cells" or the method of producing cultured cells for implantation at the site of a bone infirmity by transfecting the cells with recombinant bone morphogenic protein of WO 96/39431 which recites at page 19 "cells from a patient may be engineered with a polynucleotide (DNA or RNA) encoding a polypeptide *ex vivo*, with the engineered cells then being provided to a patient to be treated with the polypeptide", with the interchangeable BMP-2 protein of US Pat No. 5,645,084 or the interchangeable BMP-2 protein of US Pat No. 5,700,774 because all of the references taught the advantageous use of BMPs for treatment of bone infirmities by stimulating progenitor cells to proliferate. BMP-2 was taught to be produced recombinantly and to produce proliferation and differentiation in bone progenitor cells in US Pat No. 5,645,084. US Pat No. 5,645,084 also taught that BMP's are shown to be interchangeable for the use of treating a bone infirmity. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US Pat No. 5,763,416 or WO 96/39431 with US Pat No. 5,645,084 and US Pat No. 5,700,774.

Response to Arguments

9. Arguments set forth in Paper No. 15 assert that the amendment in Paper No. 15 to claim 11 has avoided the rejection of the claims over WO 96/39431 since the claims are now drawn to BMP-2 and WO 96/39431 teaches BMP-10. This is not found convincing since the obviousness of the teachings of WO 96/39431 are still relevant given the teachings of US Pat No. 5,763,416,

US Pat No. 5,645,084 and US Pat No. 5,700,774. WO 96/39431 teaches the use of a BMP protein which has been produced by recombinant means used in a method of treatment of a bone deformity by acting on bone progenitor cells to proliferate and differentiate.

10. Arguments set forth in Paper No. 15 assert that apoptosis appeared to be less in cells transfected with an adenovirus vector encoding BMP-2. The reduction is apoptosis which is taught in the specification at page 47 teaches that apoptosis "decreases with time". This is a logically expected result of the induction of proliferation and differentiation. A reduction in apoptosis is an expected result of induction of proliferation and differentiation.

11. Arguments set forth in Paper No. 15 assert that the addition of BMP-2 to cells produced a "positive effect on differentiation and proliferation". This is expected, given the teachings of the prior art in the rejection above that BMP-2 produces proliferation and differentiation.

12. Arguments set forth in Paper No. 15 assert that the instant invention presents "unexpectedly improved results over the prior art BMP expression systems". This is not found convincing, since BMP's of the prior art of the above rejection also taught an increase of proliferation and differentiation. No showing of unexpected results is found in the specification over these teachings.

Conclusion

13. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of

such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

William Sandals, Ph.D.

Examiner

June 14, 2001

TERRY MCKELVEY
PRIMARY EXAMINER